

E4
m is 0 or 1;
C is carbon or substituted carbon when G is a single or double bond;
J is carbonyl or a heteroatom moiety, wherein the heteroatom is selected from the group consisting of nitrogen, silicon, phosphorus, sulfur; and
G is a bond selected from single, double or triple bonds, wherein when G is a single bond, two R groups are attached to each C, and when G is a double bond, one R group is attached to each C, wherein R is a substitution group.

REMARKS

Claims 47 and 48 are allowed. Claims 57-67 are pending. Claims 68-71 are newly added. Support for new claims 68-71 is found in the specification at page 25, line 16 through page 26, line 13.

Title of the Invention

The Examiner states that the title provided in the previous response, "Electrodes Linked Via Conductive Oligomers to Nucleic Acids and Electron Transfer Moieties" is not clearly indicative of the invention. Applicants have amended the title to be descriptive of the invention. Accordingly, Applicants respectfully request withdrawal of the rejection.

Drawings

Applicants acknowledge the Examiner's reminder that the required time for filing corrected drawings has changed. A set of corrected drawings is enclosed. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C § 112, first paragraph

Claims 62-67 stand rejected under 35 U.S.C § 112, first paragraph as containing New Matter as a result of the amendment filed November 20, 2001. Specifically, the Examiner has found no structural limitations to connect the components in the claims 62 and 66.

Claims 62 and 66 have been amended to include structural limitations to connect the components. Specifically, as amended, the claims recite a nucleoside analog covalently attached to a conductive oligomer with a metallocene (see page 33, lines 6 -16).

Accordingly, Claims 62 and 66 as amended and their dependent claims 63-65 and 67 do not contain New Matter. Applicants respectfully request a withdrawal of this rejection.

Rejection under 35 U.S.C § 112, second paragraph

Claims 62-67 stand rejected under 35 U.S.C § 112, second paragraph, as being indefinite.

As explained above, Claims 62 and 66, have been amended to to include structural limitations to connect the components.

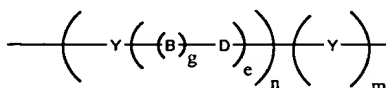
Accordingly, Applicants respectfully request a withdrawal of this rejection.

Rejection under 35 U.S.C § 102 (e)

Claim 57 stands rejected under 35 U.S.C § 102(e) as being anticipated by Marble et al. (U.S. Patent No. 5,700,667).

Marble et al. teach a method of preparing immobilized DNA in which the DNA is covalently linked to controlled pore glass (CPG) via a 3'-O-succinyl-ester.

Claim 57 is directed to a composition comprising a conductive oligomer covalently attached to a CPG-nucleoside. As amended, Claim 57 discloses a conductive oligomer having the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group; and

wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

There is no disclosure in Marble of a conductive oligomer having the formula recited in Claim 57.

An anticipation rejection requires that a single reference expressly or inherently disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). Additionally, the reference must enable and describe the claimed invention “sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention.” 31 USPQ2d at 1673. To be enabling, the reference must teach the skilled artisan how to make and use the full scope of the claimed invention without undue experimentation. *See Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997).

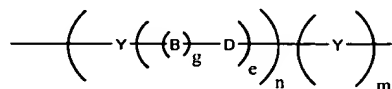
As can be seen from the above discussion, although Marble *et al.*, disclose DNA covalently linked to CPG, Marble *et al.*, does not teach a composition comprising a conductive oligomer having the formula recited in Claim 57. Therefore, Marble, *et al.*, does not teach or suggest each and every element of the claimed invention. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of Claim 57 under 35 U.S.C. § 102(e) as being anticipated by Marble, *et al.*

Rejection under 35 U.S.C § 103 (a)

Claims 62-65 stand rejected under 35 U.S.C § 103(a) as being unpatentable over Sargent *et al.* (U.S. Patent No. 5,601,982).

Sargent *et al.* teach a method for determining the sequence of nucleic acids using scanning tunneling microscopy. In order to sequence nucleic acids using scanning tunneling microscopy, a nucleic acid molecule is labeled with a base specific label that allows the labeled base to be distinguished from adjacent base. Both the labels and methods of synthesizing chemically or enzymatically modified nucleic acids are those generally known to those in the art. Thus, Sargent *et al.*, use methods known to those of skill in the art to provide nucleic acids labeled with suitable labels that can be used for sequencing nucleic acids using scanning tunneling microscopy. See column 2, lines 4-41. Sargent *et al.* do not teach or suggest the use of conductive oligomers

Claims 62-65 are directed to compositions comprising a phosphoramidite nucleoside covalently attached to a metallocene and covalently attached to a conductive oligomer having the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group; and

wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

When rejecting claims under 35 U.S.C. § 103, the Examiner bears the burden of establishing a *prima facie* case of obviousness. *See, e.g., In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993); M.P.E.P. § 2142. To establish a *prima facie* case, three basic criteria must be met, one of which is that the prior art must provide one of ordinary skill with a suggestion or motivation to modify or combine the teachings of the references relied upon by the Examiner to arrive at the claimed invention. Additionally, the teaching or suggestion to make the claimed invention, as well as the reasonable expectation of success, must come from the prior art, not Applicant's disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); M.P.E.P. § 706.02(j).

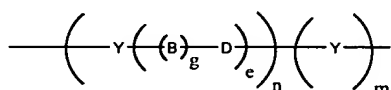
It is clear that Sargent et al. does not provide a suggestion or motivation to modify their invention to covalently attach a conductive oligomer having the formula disclosed in claim 62. Further, this reference does not teach or suggest every claim limitations, i.e. conductive oligomers having the formulas disclosed in Claim 62 or newly added claim 70. Therefore, Applicants respectfully submit that a *prima facie* case of obviousness has not been established and the rejection should be withdrawn.

Claims 58, 60, and 61 stand rejected under 35 U.S.C § 103(a) as being unpatentable over Heller et al. (U.S. Patent No. 5,849,486).

Heller *et al.* reports a method for concentrating and reacting analytes at specific microlocations (column 11, lines 9-11). This is accomplished by using electrophoretic forces to transport charged compounds (column 10, lines 25-33). This method uses electrodes

covered by a permeation layer (column 12, lines 26-27). The permeation layer precludes DNA from contacting the electrode directly (column 10, lines 6-9). The purpose of the permeation layer is to allow passage of ions sufficient for electrophoresis but to prevent the destruction of the nucleic acids attached to the "outer" surface of the permeation layer. The permeation layer can be formed using materials such as metal oxides, ceramics, carbon polymers and glass (column 12, line 27-31 and column 17, line 64 to column 18, line 6).

In contrast, claim 58 is directed to an electrode comprising a monolayer comprising a passivation agent layer comprising conductive oligomers having the formula shown below, and at least one nucleic acid covalently attached to the electrode with a spacer.



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group; and

wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

As discussed above, the Examiner has the burden to establish a *prima facie* case of obviousness when rejecting claims under 35 U.S.C. §103(a). It is clear that Heller et al. does not provide a suggestion or motivation to modify their invention to covalently attach a conductive oligomer having the formula disclosed in claim 58. Further, this reference does not teach or suggest every claim limitations, i.e. conductive oligomers having the formulas disclosed in Claim 58 or newly added claim 69. Therefore, Applicants respectfully submit that a *prima facie* case of obviousness has not been established and the rejection should be withdrawn.

Objection to Claim 59

Claim 59 is objected to as being dependent upon a rejected base claim, Claim 58. As discussed above, Applicants submit that the rejection of the base claim, Claim 58, should be withdrawn. Therefore, the objection to Claim 59 should be withdrawn.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current Amendment". The attached page is captioned **"Version with markings to show changes made."**

The applicants submit that the claims are now in condition for allowance and an early notification of such is respectfully solicited. If after review, the Examiner feels that there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

Dated: 5/16/02

Respectfully submitted,

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In the Title

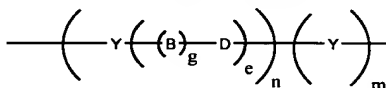
The title beginning at line 1 of page 1 has been amended as follows:

~~ELECTRODES LINKED VIA CONDUCTIVE OLIGOMERS TO NUCLEIC
ACIDS AND ELECTRON TRANSFER MOIETIES ATTACHED TO
ELECTRODES AND NUCLEOSIDE ANALOGS~~

In the claims:

Claim 57 has been amended as follows:

57. (Amended) A composition comprising a conductive oligomer covalently attached to a CPG-nucleoside, wherein said conductive oligomer has the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group;

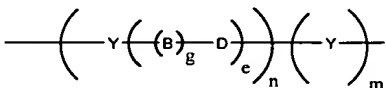
and

wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

Claim 58 has been amended as follows:

58. (Amended) An electrode comprising:

a) a monolayer comprising a passivation agent layer comprising conductive oligomers, wherein said conductive oligomer having the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

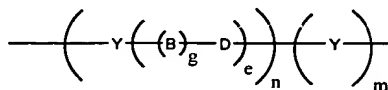
wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-,

wherein R is a substitution group; and

- wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus; and,
b) at least one nucleic acid covalently attached to said electrode with a spacer.

Claim 62 has been amended as follows:

62. (Amended) composition comprising a phosphoramidite nucleoside covalently attached to a conductive oligomer with a metallocene ligand, wherein said conductive oligomer has the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10;and

m is zero or 1;

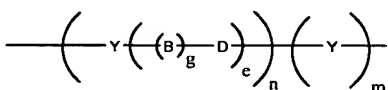
wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group;

and

wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

Claim 66 has been amended as follows:

66. (Amended) A composition comprising a deoxynucleotide triphosphate covalently attached to a conductive oligomer with a metallocene ligand, wherein said conductive oligomer has the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10;and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group;

and

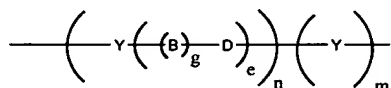
wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

Appendix of Pending and Allowed Claims

47. (Allowed) A conductive oligomer comprising an ethyl-pyridine protected sulfur atom.

48. (Allowed) A conductive oligomer comprising a trimethylsilylethyl protected sulfur atom.

57. (Amended) A composition comprising a conductive oligomer covalently attached to a CPG-nucleoside, wherein said conductive oligomer has the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

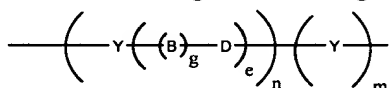
m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group; and

wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

58. (Amended) An electrode comprising:

a) a monolayer comprising a passivation agent layer comprising conductive oligomers, wherein said conductive oligomer having the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group; and

wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus; and,

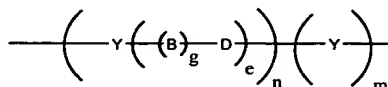
b) at least one nucleic acid covalently attached to said electrode with a spacer.

59. A composition according to claim 58 wherein said spacer is a conductive oligomer.

60. A composition according to claim 58 wherein said spacer is an insulator.

61. A composition according to claim 58 wherein said passivation agent layer further comprises insulators.

62. (Amended) composition comprising a phosphoramidite nucleoside covalently attached to a conductive oligomer with a metallocene ligand, wherein said conductive oligomer has the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group; and

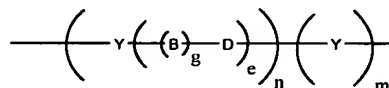
wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

63. A composition according to claim 62 wherein said nucleoside comprises a ribose and said metallocene is covalently attached to the 2' position of said ribose.

64. A composition according to claim 62 wherein said metallocene is covalently attached to the base of said nucleoside.

65. A composition according to claim 62 wherein said metallocene is ferrocene.

66. (Amended) A composition comprising a deoxynucleotide triphosphate covalently attached to a conductive oligomer with a metallocene ligand, wherein said conductive oligomer has the formula:



wherein

Y is an aromatic group;

n is an integer from 1 to 50;

g is either 1 or zero;

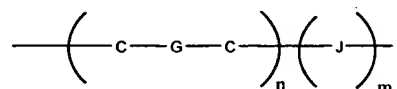
e is an integer from zero to 10; and

m is zero or 1;

wherein when g is 1, B-D is selected from acetylene, alkene, substituted alkene, amide, azo, esters, thioesters, -CH=N-, -CR=N-, -N=CH- and -N=CR-, -SiH=SiH-, -SiR=SiH-, -SiR=SiH-, and -SiR=SiR-, -SiH=CH-, -SiR=CH-, -SiH=CR-, -SiR=CR-, -CH=SiH-, -CR=SiH-, -CH=SiR-, and -CR=SiR-, wherein R is a substitution group; and
 wherein when g is zero, e is 1 and D is carbonyl or a moiety comprising oxygen, sulfur, nitrogen or phosphorus.

67. A composition according to claim 66 wherein said metallocene is ferrocene.

68. (New) A composition according to claim 57 wherein said conductive oligomer has the formula:



wherein

n is an integer from 1 to 50;

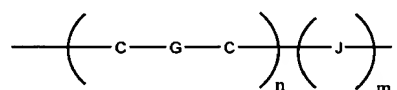
m is 0 or 1;

C is carbon or substituted carbon when G is a single or double bond;

J is carbonyl or a heteroatom moiety, wherein the heteroatom is selected from the group consisting of nitrogen, silicon, phosphorus, sulfur; and

G is a bond selected from single, double or triple bonds, wherein when G is a single bond, two R groups are attached to each C, and when G is a double bond, one R group is attached to each C, wherein R is a substitution group

69. (New) A composition according to claim 58 wherein said conductive oligomer has the formula:



wherein

n is an integer from 1 to 50;

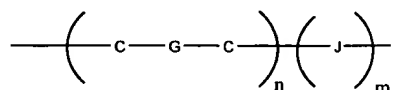
m is 0 or 1;

C is carbon or substituted carbon when G is a single or double bond;

J is carbonyl or a heteroatom moiety, wherein the heteroatom is selected from the group consisting of nitrogen, silicon, phosphorus, sulfur; and

G is a bond selected from single, double or triple bonds, wherein when G is a single bond, two R groups are attached to each C, and when G is a double bond, one R group is attached to each C, wherein R is a substitution group.

70. (New) A composition according to claim 62 wherein said conductive oligomer has the formula:



wherein

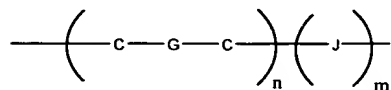
n is an integer from 1 to 50;

m is 0 or 1;

C is carbon or substituted carbon when G is a single or double bond;

J is carbonyl or a heteroatom moiety, wherein the heteroatom is selected from the group consisting of nitrogen, silicon, phosphorus, sulfur; and
 G is a bond selected from single, double or triple bonds, wherein when G is a single bond, two R groups are attached to each C, and when G is a double bond, one R group is attached to each C, wherein R is a substitution group.

71. (New) A composition according to claim 66 wherein said conductive oligomer has the formula:



wherein

n is an integer from 1 to 50;

m is 0 or 1;

C is carbon or substituted carbon when G is a single or double bond;

J is carbonyl or a heteroatom moiety, wherein the heteroatom is selected from the group consisting of nitrogen, silicon, phosphorus, sulfur; and

G is a bond selected from single, double or triple bonds, wherein when G is a single bond, two R groups are attached to each C, and when G is a double bond, one R group is attached to each C, wherein R is a substitution group.